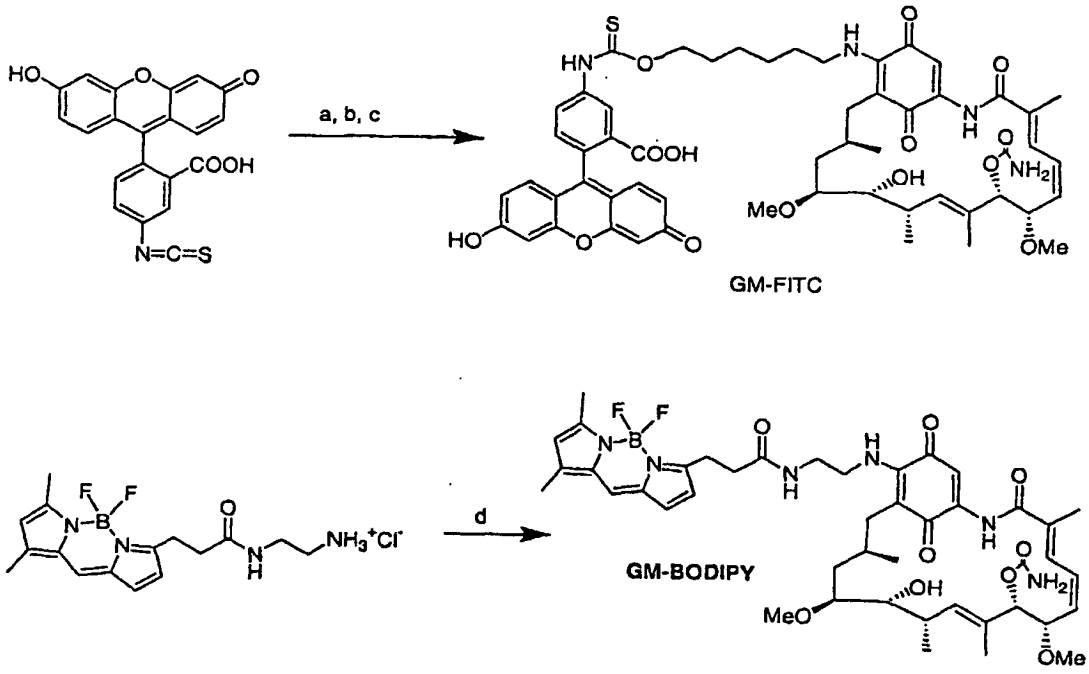


Scheme 1. Synthesis of the GM-fluorescent ligands. (a) 6-(Boc-amino-)-1-hexanol, TEA, DMF, 60 °C, 24 h; (b) TFA/CH_2Cl_2 (1:4), 45 min, rt; (c) GM, TEA, DMF, rt, 24 h; (d) GM, DIEA, CH_2Cl_2, rt, 24 h.

Fig. 1

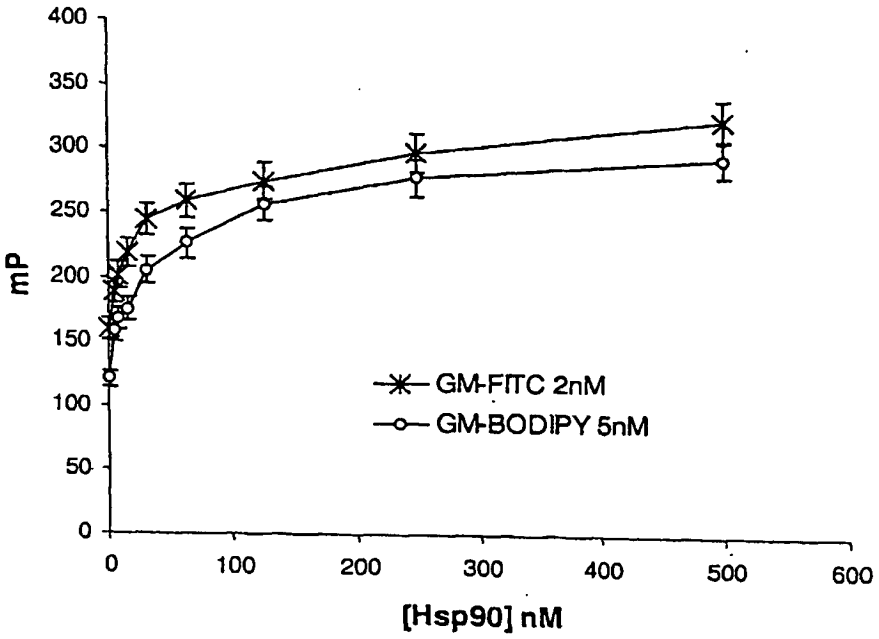
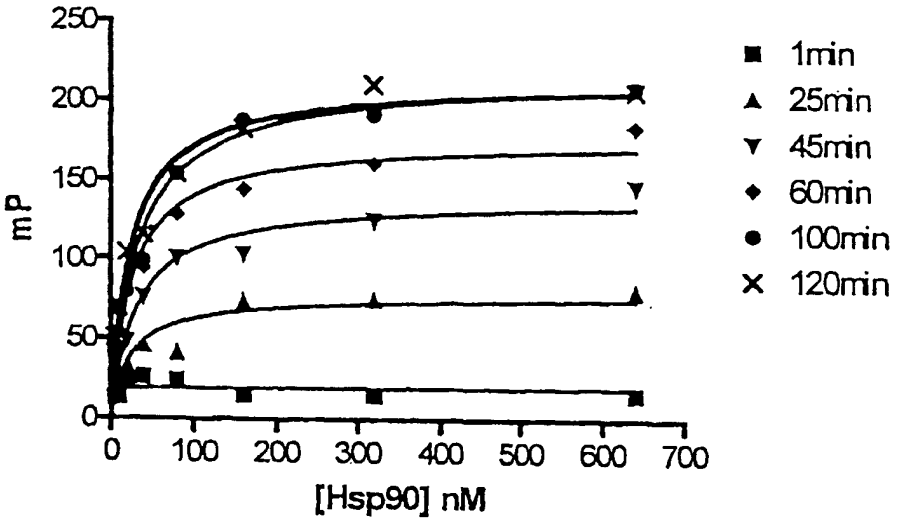


Fig. 2

Fig. 3


250
200
150
100
50
0
mP
0
100
200
300
400
500
600
700
[Hsp90] nM
1min
25min
45min
60min
100min
120min

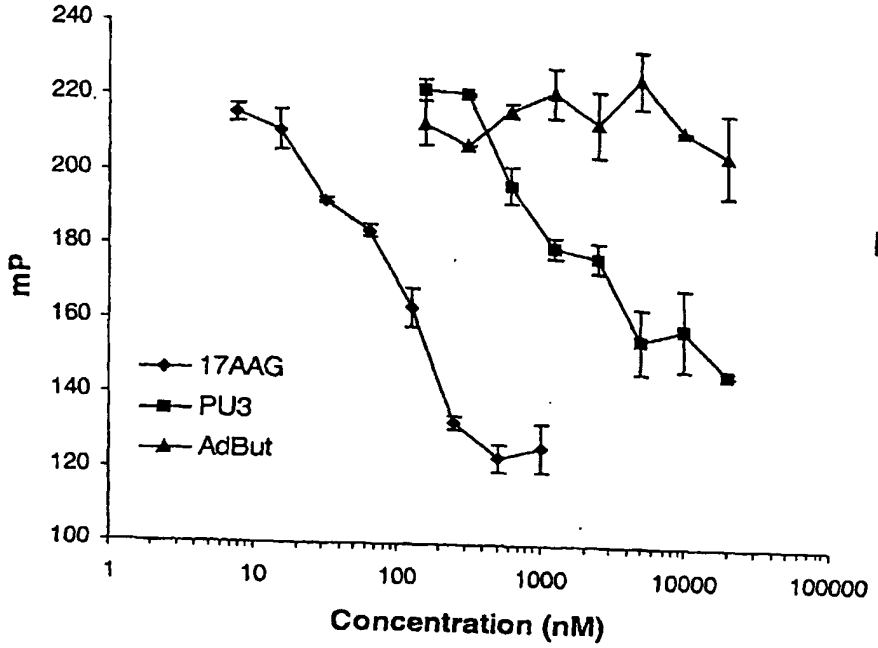

240
220
200
180
160
140
120
100
mP
17AAG
PU3
AdBut
1
10
100
1000
10000
100000
Concentration (nM)

Fig. 4

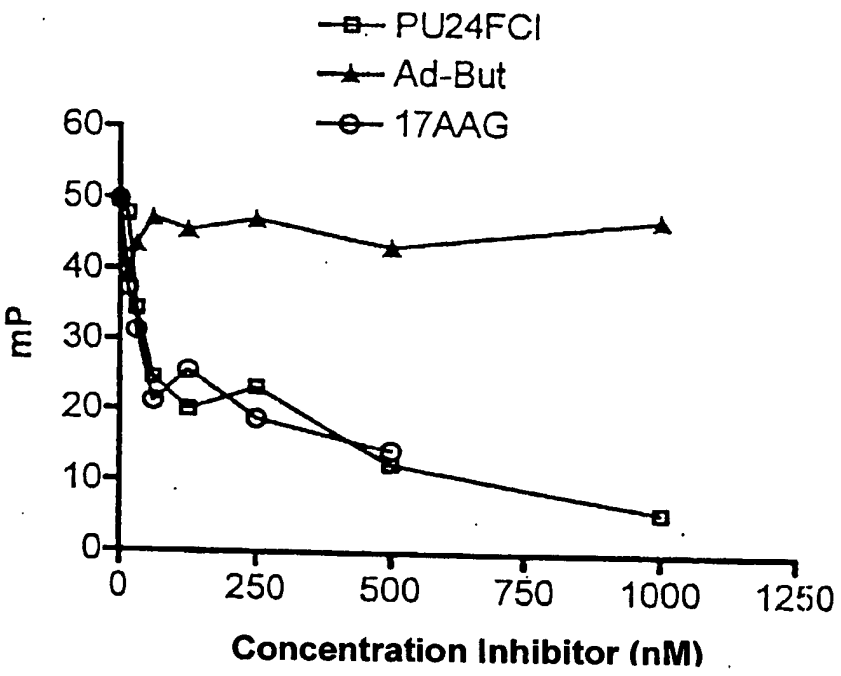

PU24FCl
Ad-But
17AAG
mP
60
50
40
30
20
10
0
0
250
500
750
1000
1250
Concentration Inhibitor (nM)

Fig. 5

B

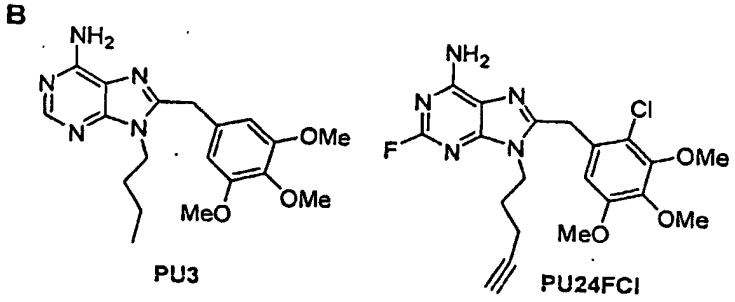

NH2
N
N
N
N
OMe
MeO
OMe
PU3
NH2
N
N
F
N
N
Cl
OMe
MeO
OMe
PU24FCl

Fig. 6

Fig. 7A

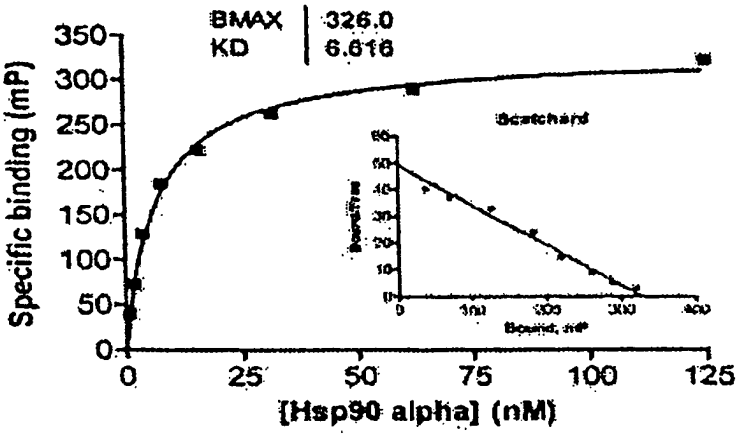


Fig. 7B

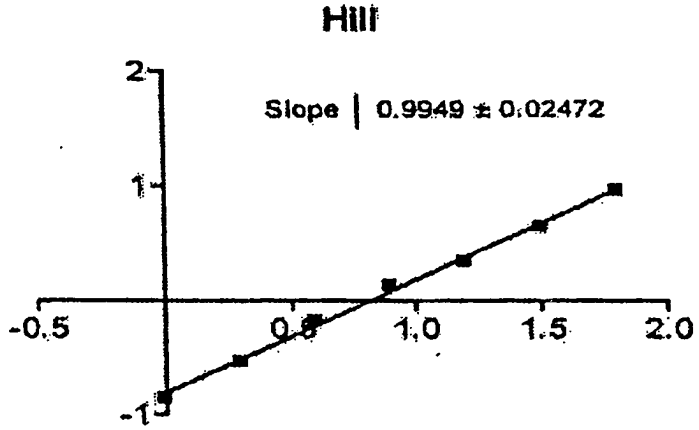
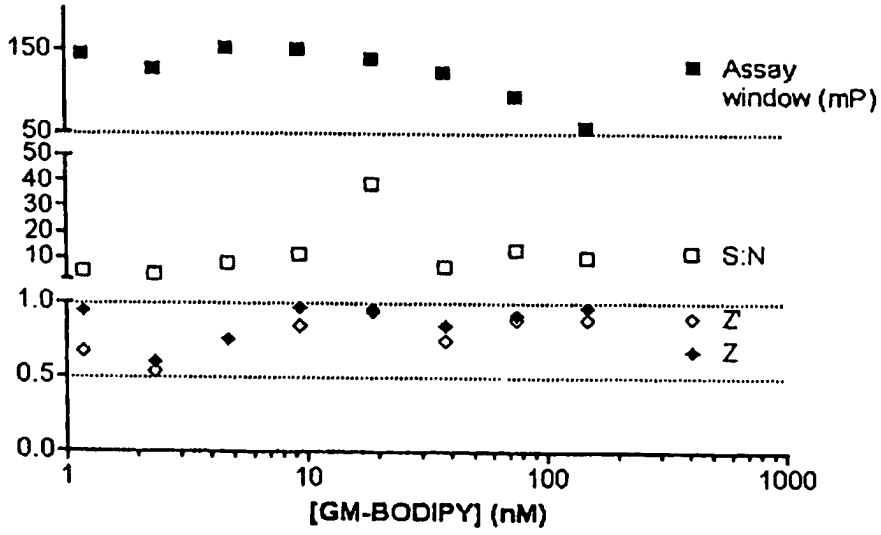


Fig. 7C



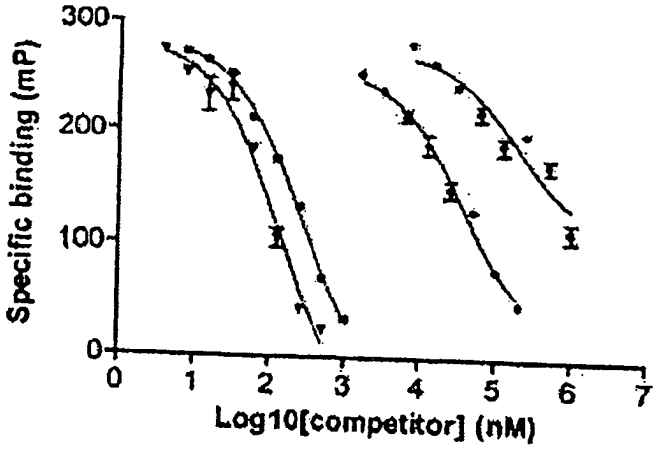


Fig. 8

Fig. 9A

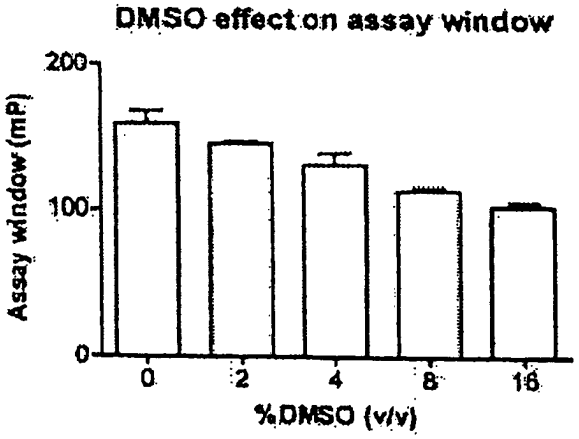
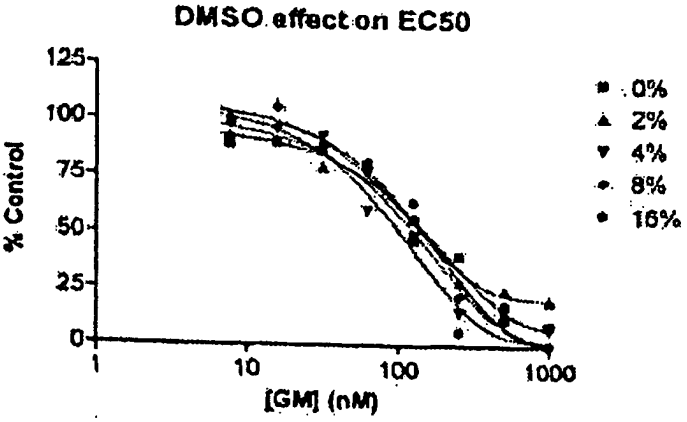


Fig. 9B



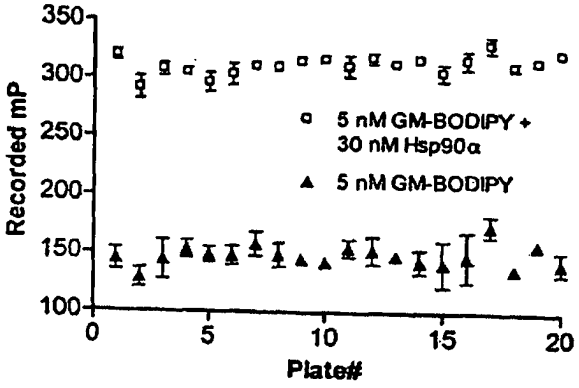


Fig. 10 A

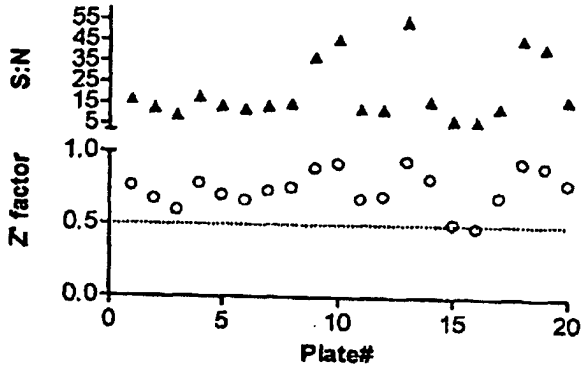


Fig. 10B

	Brain	K562	SKBr3
Sigmoidal dose-response			
Best-fit values			
BOTTOM	137.2	137.2	131.8
TOP	540.9	275.8	306.4
LOGEC50	1.233	-0.1382	0.1423
EC50	17.11	0.7274	1.388

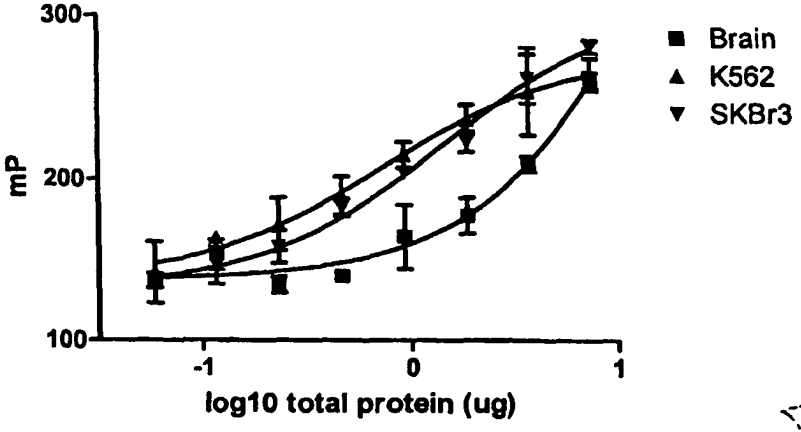


Fig. 11

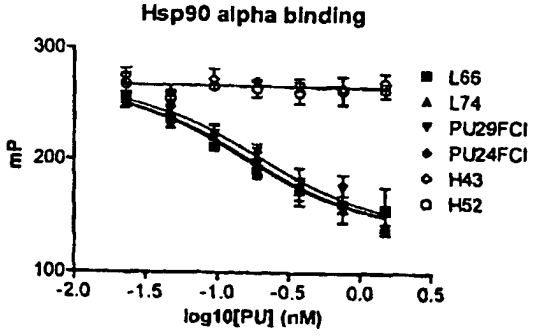


Fig. 12A

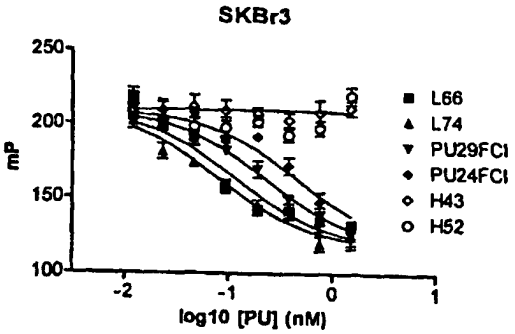


Fig. 12B

Fig. 13A

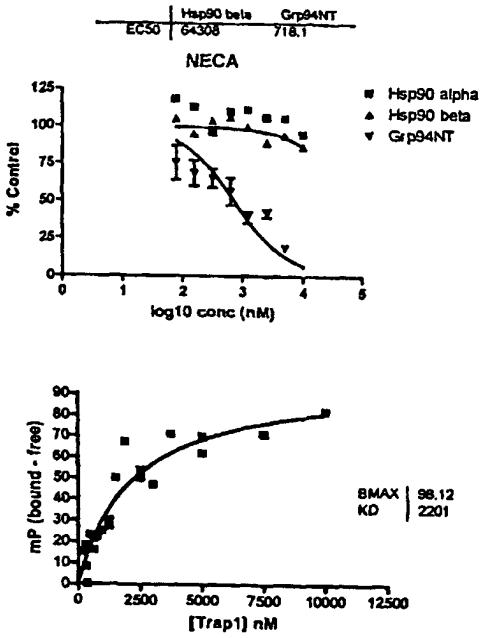


Fig. 13B

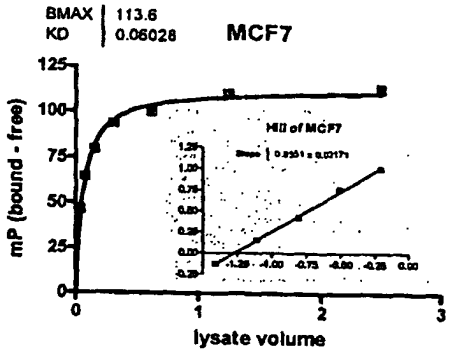


Fig. 13C

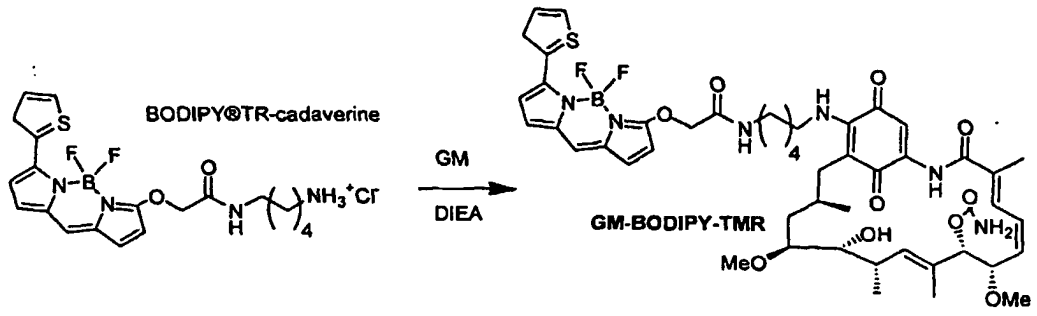


Fig. 14

Fig. 15A

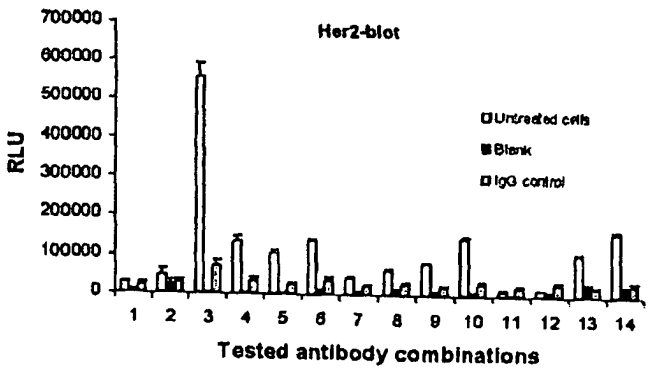
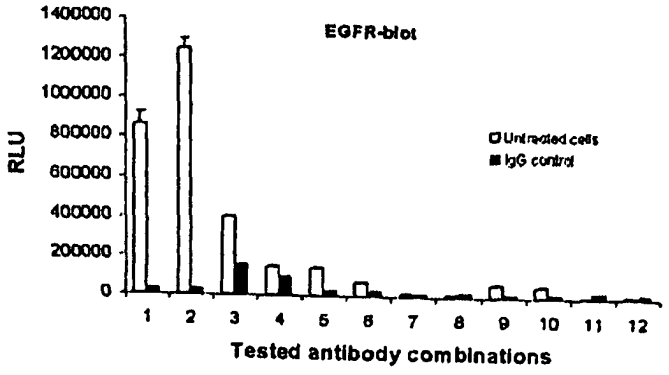


Fig. 15B



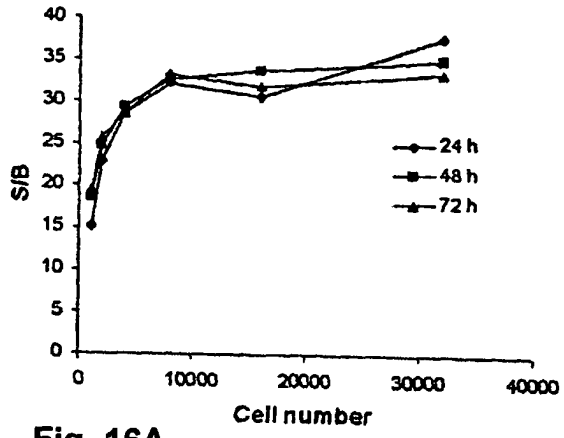


Fig. 16A

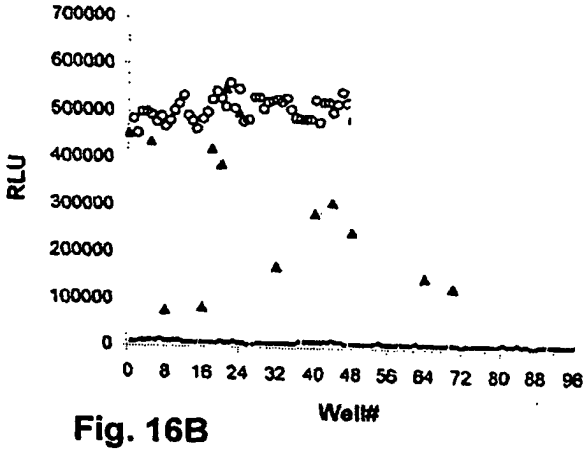


Fig. 16B

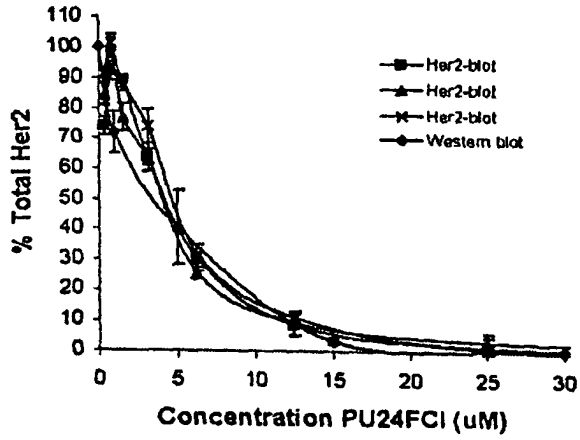


Fig. 17

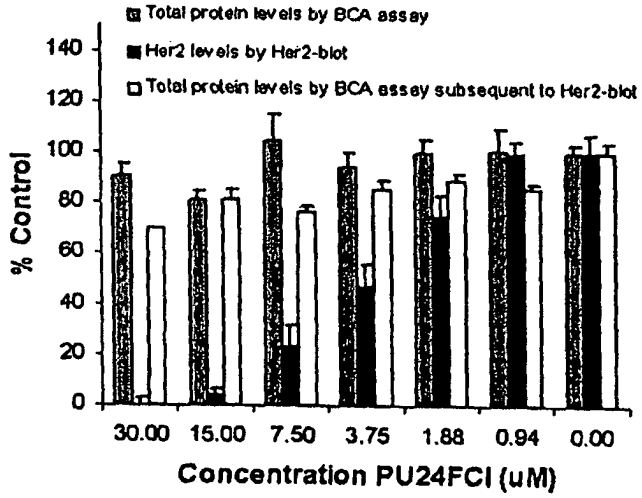


Fig. 18A

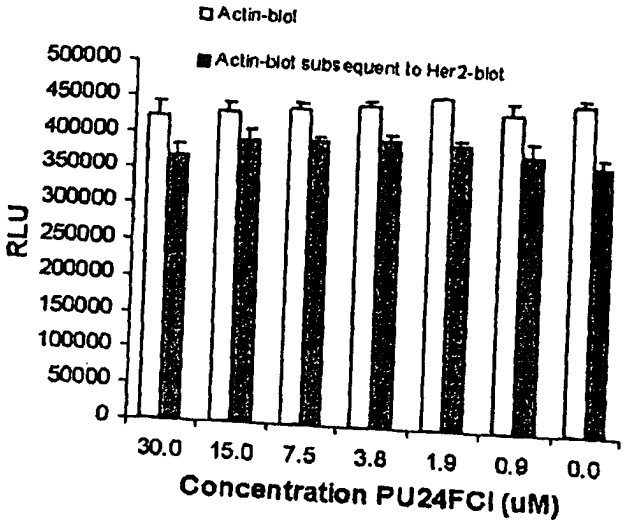


Fig. 18B

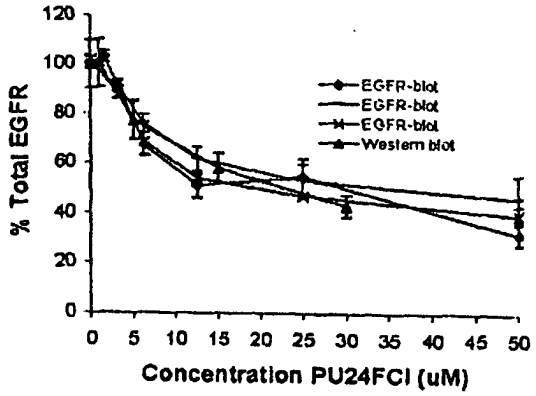


Fig. 19

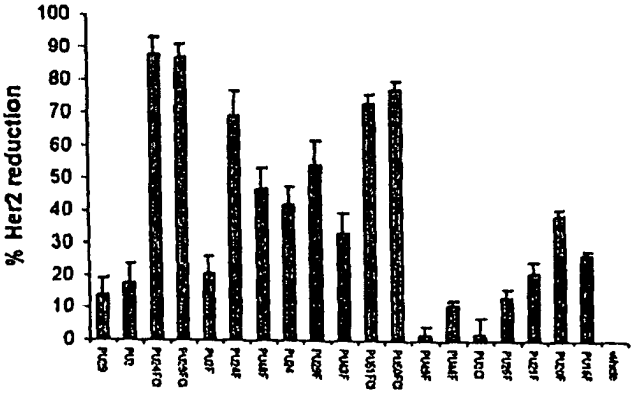


Fig. 20

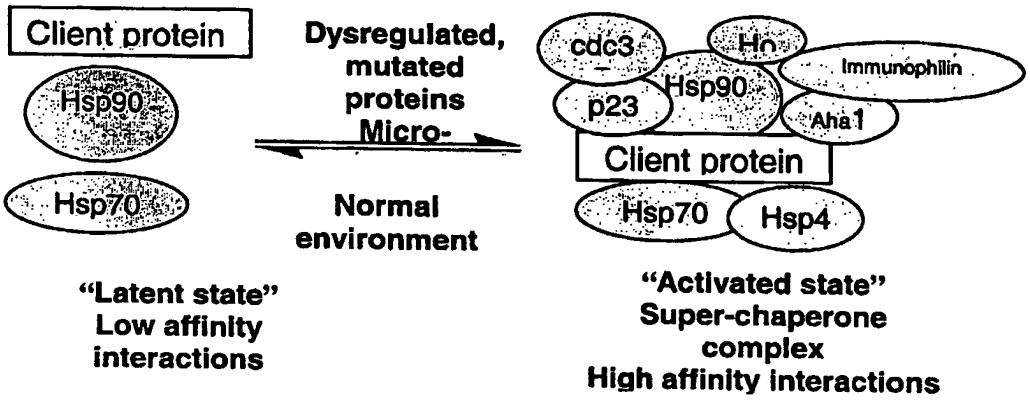

Client protein
Hsp90
Hsp70
Dysregulated, mutated proteins Micro-
Normal environment
cdc3
Hn
Immunophilin
Hsp90
p23
Aha1
Client protein
Hsp70
Hsp4
"Latent state" Low affinity interactions
"Activated state" Super-chaperone complex High affinity interactions

Fig. 21

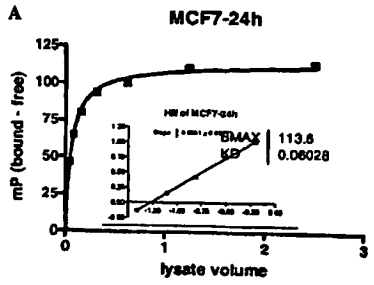


Fig. 22A

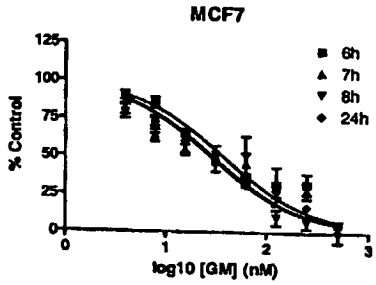


Fig. 22B

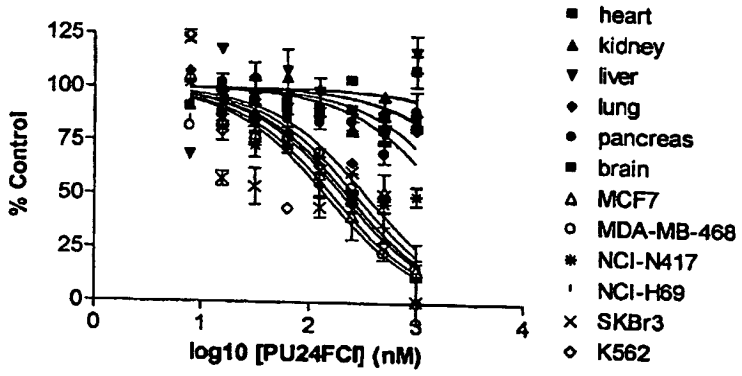


Fig. 22C

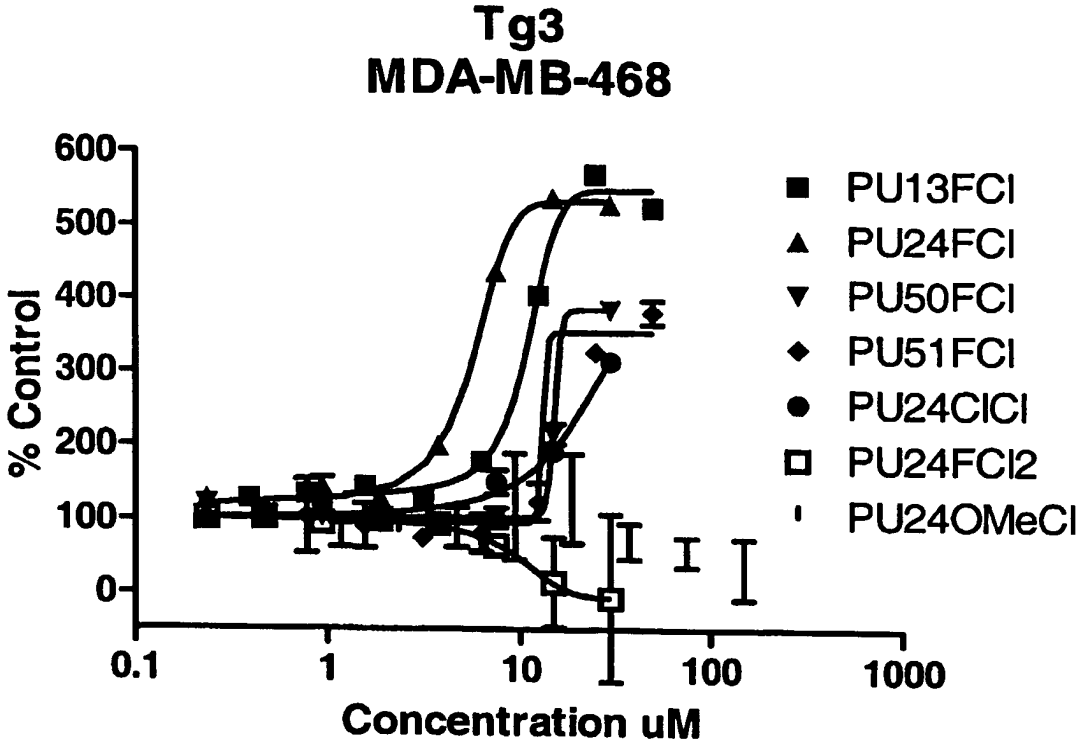

Tg3
MDA-MB-468
600
500
400
300
200
100
0
% Control
0.1
1
10
100
1000
Concentration uM
PU13FCl
PU24FCl
PU50FCl
PU51FCl
PU24ClCl
PU24FCl2
PU24OMeCl

Fig. 23

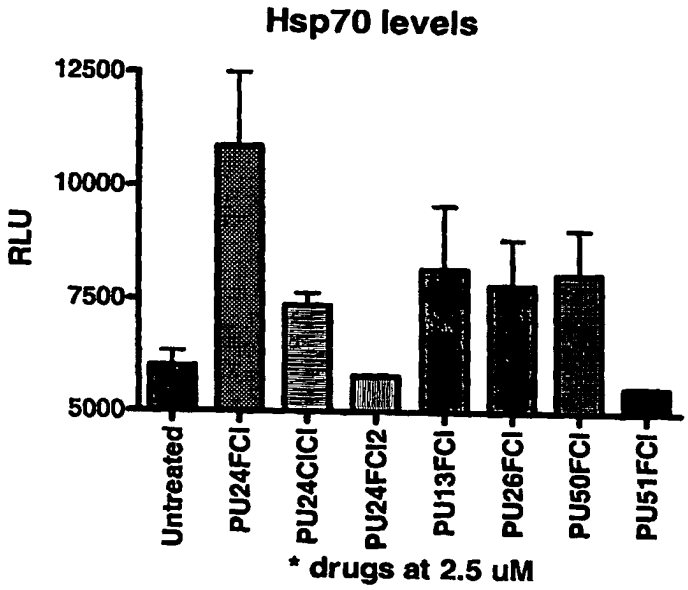

Hsp70 levels
RLU
12500
10000
7500
5000
Untreated
PU24FCl
PU24ClCl
PU24FCl2
PU13FCl
PU26FCl
PU50FCl
PU51FCl
* drugs at 2.5 uM

Fig. 24